REMARKS

The Office Action mailed August 17, 2010, was reviewed and the comments of the Patent and Trademark Office were considered.

Claims 1, 4, 5, 7 - 19, and 22 - 39 are pending. Claims 2, 3, 6, 20 and 21 are canceled without prejudice. Claims 1, 7, 8, 12 - 14 and 28 are currently amended. Support for the amendments can be found in the original claims and the specification generally. Applicants respectfully submit that no new matter has been added by the amendments.

Withdrawal of the rejections and allowance of all claims are respectfully requested.

CLAIM OBJECTIONS

Applicants have amended dependent claim 7 to indicate the upper limit. No new matter has been added by the amendment.

Applicants have amended dependent claim 28 to correct the dependency issue. No new matter has been added by the amendment.

DOUBLE PATENTING REJECTION

Claims 1, 4, 5, 7-19, 22-23, 28 and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 12-22, 25, 26, 28, 29, 35 and 36 of copending Application No. 10/580,035.

As neither this application nor the cited application have received indications of allowable subject matter, Applicants respectfully request that the provisional rejection be held in abeyance until such time.

Claims 1, 4, 5, 7-19, 22-23, 28, 29 and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20, 25 and 27 of copending Application No. 11/878,947, over claims 1-16, 21, 22, 24-26, 28 and 29 of

copending Application No. 10/580,023, over claims 1-3, 5-16, 19, 21, 22, 24-26, 28 and 29 of copending Application No. 11,808,456, over claims 1-10, 16, 18-24 of the US Patent 7,683,024 and over claims 1-4, 6-11, 15, 16, 18-21, 26-30, 38 and 39 of copending Application 12/003,095.

As neither this application nor the cited application have received indications of allowable subject matter, Applicants respectfully request that the provisional rejection be held in abeyance until such time.

Claims 1, 4, 5, 7-19, 22-23, 28, 29, and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21, 28-32 and 40 of Huille et al. (US Patent No. 6,630,171), in view of each Regalado et al. (Macromolecules, 1999, 32: 8580-8588), Dupuis et al. (US Patent No. 6,607,714), and Bromberg et al. (US Patent No. 5,939,485).

Applicants amended claim 1 to recite that the polymer is a polyamino acid formed of aspartic units and/or glutamic units. Therefore, Applicants state that claim 1 is now directed to a specific polyamino acid formulation for the prolonged delivery of interferon. The cited references, namely US Patent No. 6,630,171 in view of Regalado, Dupuis and Bromberg do not disclose every element of the claimed invention, and, therefore, the claimed invention is patentably distinct from the cited references.

For example, at page 8, the Examiner argues that Regalado discloses incorporation of HG into hydrophilic polymers to create amphiphilic polymers that are capable of sol to gel transition depending on amphiphilic polymer concentration (p. 8580, C. 1; p. 8587, C. 2). It was well-known in the art that amphiphilic polymers are capable of sol to gel transition. The current invention is not directed to gelling of amphiphilic polymer, but to the existence of a relation between the concentration C1 of the polyamino acid and an increase in the release time of interferon(s). This relation was not obvious and one skilled person would not have found in Regalado how to determine the critical concentration C1 of the polymer PO making it possible to prolong and control the in vivo release time of the interferon(s) beyond 24 h after administration. Regalado does not teach an increase in the release time of active principle because the polymer of Regalado is not used to carry active principle. Determining the critical concentration during an IG test is a way to obtain the accurate release time. Therefore, Regalado does not teach how to obtain the accurate release time.

At page 8, the Examiner argues that Dupuis et al. teach amphiphilic polymer solutions which are capable of forming gels in the presence of serum proteins such as albumin (Examples 4 and 5). First, Applicants state that the composition of the claimed invention does not contain itself bovine serum albumin (BSA). In fact, the pharmaceutical composition must be liquid to be administered by injection. Thus, no BSA should be added to the formulation before the injection. Examples 4 and 5 of Dupuis are related to various compositions comprising variable concentrations of amphiphilic polymer and variable concentrations of BSA. Indeed, Dupuis discloses how to determine the BSA concentration which gives rise to gelation of the aqueous medium (see example 5, column 10). However, Dupuis does not teach how to prolong the in vivo release time of the interferon(s) beyond 24 h after administration, more particularly it does not teach the polyamino acid of claim 1and how to determine the critical concentration C1 of this polyamino acid.

It is to Applicants' credit to have developed and fine-tuned an IG test allowing ascertaining a suitable concentration C1 of polyamino acid. Dupuis does not anticipate the existence of a critical concentration for which the release time is greatly increased.

Additionally, Dupuis does not disclose how to perform the IG test to determine the critical concentration. The relation between this critical concentration C1 of the polymer PO and the significant increase in the release time is not disclosed in Dupuis. For at least these reasons, the current claims are patentably distinct from Dupuis (US Patent No. 6,607,714). Applicants respectfully requests the rejection be withdrawn.

At page 8, the Examiner argues that Bromberg et al. teach the necessity of using responsive polymers capable of forming a gel in the presence of an environmental stimulus. On the contrary, the current invention was designed to obtain a liquid pharmaceutical formulation comprising an aqueous colloidal suspension of polyamino acid that can delay the release of the interferon, without using stimuli such as temperature or pH change. Bromberg teaches a way to control the gelation of some types of polymer, namely polyoxyalkylene, but does not teach any relation between a concentration of polymer and the increase in the release time of interferon in vivo. For these reasons, Bromberg does not render the currently amended first claim obvious. The Applicant respectfully requests the rejection be withdrawn.

Claims 1, 4, 5, 7-19, 22-23, 28, 29 and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 12-22 of copending Application No. 11/658,803.

The Examiner argues that the application claims are drawn to the same polymer formulation for prolonged delivery of interferon, wherein the polymer is capable of forming a gel upon administration in vivo. Applicants respectfully disagree because the gel disclosed in copending Application No. 11/658,803 does not form upon administration in vivo but instead is the final form of the formulation before administration to the patient. In contrast, the final form of the claimed formulation is liquid under the injection conditions, as recited in claim 1. Therefore, the final forms claimed in claim 1-10 and 12-22 of copending Application No. 11/658,803 and in the instant application are distinct.

Moreover, copending Application No. 11/658,803 does not teach how to determine the critical concentration of the polyamino acid for which the in vivo release time of the interferon(s) is prolonged beyond 24 h after administration. For at least these reasons, the current claims are patentably distinct from copending Application No. 11/658,803. Applicants respectfully request the rejection be withdrawn.

Claims 1, 4, 5, 7-19, 22-23, 28, 29 and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-25 of copending Application No. 10/558,617.

The Examiner states that the application claims are drawn to the same polymer formulation, which is capable of forming a gel upon administration in vivo. For the reasons discussed above, the final forms claimed in claim 3-25 of copending Application No. 10/558,617 and in the instant application are patentably distinct. Applicants respectfully request the rejection be withdrawn.

Claims 1, 4, 5, 7-19, 22-23, 28, 29 and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 7,659,365 in view of Regalado, Dupuis and Bromberg.

The Examiner states that the prior art suggests that the patent polymer is capable of forming a gel in vivo. The claimed invention is not directed to a way to obtain a gel in vivo but

to a formulation which permits to prolong and control the release of interferon beyond 24 h after administration. None of the cited references anticipate the existence of a critical concentration for which the release time is greatly increased.

Additionally these documents do not disclose how to determine the critical concentration. The relation between this critical concentration C1 of the polyamino acid and the significant increase in the release time is not disclosed in the prior art. As such, the current claims are patentably distinct from U.S. Patent No. 7,659,365. Applicants respectfully request the rejection be withdrawn.

Claims 1, 3-19, 21-23, 28, 29 and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 7,678,882.

U.S. Patent No. 7,678,882 does not disclose the existence of a relation between the critical concentration C1 of the polyamino acid as determined by an IG test and the significant increase in the release time of interferon(s). As such, the current claims are patentably distinct from U.S. Patent No. 7,678,882. Applicants respectfully request the rejection be withdrawn.

CLAIM REJECTIONS - 35 USC § 103

Rejection of Huille in view of Regalado

Claims 1, 4, 5, 7-8, 12-16, 18, 22, 28, 29, 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille in view of each Regalado et al. (Macromolecules, 1999, 32: 8580-8588) ("Regalado"), Dupuis et al. (U.S. Patent No. 6,607,714)("Dupuis"), and Bromberg et al. (U.S. Patent No. 5,939,485) ("Bromberg").

One of the major goals of the claimed invention is to obtain a liquid pharmaceutical formulation that can delay the release of the interferon, without using temperature or pH change. Although Huille teach a liquid formulation suitable for parenteral injection and prolonged release of interferon, Huille does not specifically teach the existence of the relation between a critical concentration C1 of the polyamino acid as determined by an IG test and the significant increase in the release time of interferon(s).

The Examiner states that Regalado teaches that incorporation of HG into hydrophilic polymers results in amphiphilic polymers which are capable of sol to gel transition depending on the amphiphilic polymer concentration. It was well-known in the art that amphiphilic polymers are capable of sol to gel transition. In the claimed invention, the formulation is liquid under the injection conditions before administration to the patient and the invention is not directed to gelling of amphiphilic polymer, but to the existence of a relation between the concentration C1 of the polyamino acid and an increase in the release time of interferon(s). This relation was not obvious and one skilled person would not have found in Regalado how to determine the critical concentration C1 of the polymer PO making it possible to prolong and control the in vivo release time of the interferon(s) beyond 24 h after administration. Regalado does not teach an increase in the release time of active principle because the polymer of Regalado is not used to carry active principle. Determining the critical concentration during an IG test is a way to obtain the accurate release time. Therefore, Regalado does not teach how to obtain the accurate release time.

The Examiner states that Dupuis teaches amphiphilic polymer solutions which are capable of forming gels in the presence of serum proteins such as albumin (Examples 4 and 5). Dupuis does not teach a polyamino acid of claim 1 and especially does not teach how to determine the critical concentration of this polymer for which the in vivo release time of the interferon(s) is prolonged beyond 24 h after administration. Therefore, Dupuis does not teach how to obtain the accurate release time and thus does not cure the deficiency of Huille.

Bromberg teaches the necessity of using responsive polymers capable of forming a gel in the presence of an environmental stimulus. On the contrary, the current invention was designed to obtain a liquid pharmaceutical formulation that can delay the release of the interferon, without using temperature or pH change. Therefore, Bromberg does not cure the deficiency of Huille.

As such, claims 1, 4, 5, 7-8, 12-16, 18, 22, 28, 29, 35-37 are patentable over Huille in view of Regalado, Dupuis, and Bromberg. Applicants respectfully request the Examiner withdraw the rejection.

Rejection of Huille in view of Regalado, Dupuis, Bromberg and Edwards.

Claims 1, 4, 5, 7-8, 12-16, 18, 22-23, 28, 29, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al. taken with Regalado, Dupuis and Bromberg, in further view of Edwards et al.(Arch. Dermatol., 1990, 126: 1029-1032, Abstract, of record) ("Edwards").

Edwards does not disclose the formation of a gel and even less a concentration of polymer that must be used to obtain the accurate release time of interferon-alpha. Therefore, Edwards does not cure the deficiency of Huille and the other cited references, and the combination does not render the instant claims obvious. Applicants respectfully request the Examiner withdraw the rejection.

Rejection of Huille in view of Regalado, Dupuis, Bromberg, Kim and Seo.

Claims 1, 4, 5, 7-8, 12-18, 22, 28, 29, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al. taken with Regalado et al., Dupuis et al. and Bromberg et al., in further view of both Kim et al. (U.S. Patent No. 5,869,703) ("Kim") and Seo et al. (U.S. Patent No. 7,311,901) ("Seo").

As noted above, Huille does not teach or suggest the existence of a relation between a gel formation in vitro and an increase in the release time of interferon(s). Kim and Seo do not teach this relation either. As such, the references alone or in combination do not render the instant claims obvious. Applicants respectfully request the Examiner withdraw the rejection.

Rejection of Huille in view of Regalado, Dupuis, Bromberg and Conover.

Claims 1, 4, 5, 7-16, 18, 22, 28, 29, and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al. taken with Regalado et al., Dupuis et al. and Bromberg et al., in further view of Conover et al. (Anti-Cancer drug Design, 1999. 14: 499-506) ("Conover").

As noted above, Huille does not teach or suggest the existence of a relation between a gel formation in vitro and an increase in the release time of interferon(s). Conover does not teach

this relation either. As such, the references alone or in combination do not render the instant claims obvious. Applicants respectfully request the Examiner withdraw the rejection.

CONCLUSION

In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing all of the claims of the present application in condition for allowance. If the Examiner believes that personal communication will expedite prosecution of this application, or should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number provided below.

Applicants believe no fee is due with this submission. If a fee is due, however, the U.S. Patent and Trademark Office is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, under Order No. 022290.0160PTUS, from which the undersigned is authorized to draw.

Dated: November 10, 2010

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